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EXAMINER	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 3

Application Number: 09/786,105
Filing Date: February 26, 2001
Appellant(s): SHIPMAN, ROBERT

Maina T.Larson
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed May 24 2004.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that claim 14 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

W

WO95/33851	DE BEENHOUWER et al.	12-1995
5,851,763	HEYM et al.	12-1998
5,985,569	FOXALL et al.	11-1999

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over De Beenhouwer et al. (WO 95/33851) and in view of Heym et al. (USPN. 5,851,763) and Foxall et al. (USPN. 5,985,569).

De Beenhouwer et al. teach a set of primers in the form of a kit to evaluate antibiotic resistance spectrum of mycobacteria, wherein the instant SEQ ID Nos. 1 and 3 match with complete homology to the primer P2 of the disclosure of De Beenhouwer et al. (see page 55, lines 17-21, page 56, lines 10-22, and page 39, line 9 (primer P2) and see sequence alignment from Gene seq database). However, DeBeenhouwer et al. did not teach SEQ ID Nos. 2 and 4.

Heym et al. teach a method and a kit for detecting mutations in antibiotic resistance mycobacterium tuberculosis wherein Heym et al. teach primers are selected from rpoB gene sequence (SEQ ID No. 59) of mycobacterium tuberculosis, which comprises the instant claimed SEQ ID Nos. 2 and 4 with complete homology (see sequence alignment from issued patent database, and column 24, lines 8-13, lines 52-56, columns 85-86, SEQ ID NO. 59 and column 3, lines 35-41).

Foxall et al. teach designing mycobacterium genus-specific primers for polymerase chain reaction using a computer program, OLIGO-PROBE DESIGN STATION (see column 13, lines 30-61).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the sequences of primer as taught by De Beenhouwer et al. with the primer selection sequence as taught by Heym et al. and Foxall et al. which is well known in

the art at the time the invention was made, because De Beenhouwer et al. states that "probes including species specific probes contained in the sequence of the rpoB gene are designed in such a way that they all can be used simultaneously, under the same hybridization conditions, which implies a single amplification and hybridization step is sufficient for simultaneous detection of rafampicin resistance and the identification of the mycobacterial species involved' (see page 16, lines 6-13). One such alternative form of sequence selection from rpoB gene, expressly motivated by Heym et al. is the design of primer sequence encompassed by rpoB gene.

Further, In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the court determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the court stated

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

Since the claimed primers simply represent structural homologs, which are suggested by the prior art as useful for primers and probes, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

An ordinary practitioner would have been motivated to combine the sequences of De Beenhouwer et al. with the primer sequences of Heym et al. and selection of primers of Foxall et al. in order to achieve the expected advantage of a sensitive kit composition for evaluating antibiotic resistance of mycobacterium species. Claim, which utilizes closed language that require the inclusion of primers 1-4 would overcome this rejection.

(11) Response to Argument

Introduction

The instant claim 14 is drawn to a kit composition for evaluation of antibiotic mutations in a sample of Mycobacterium tuberculosis, comprising pairs of amplification primers and matched pairs of sequencing primers for amplification and sequencing. SEQ ID Nos. 1-4 are elected by Applicants for examination purposes. Seq ID Nos. 1-2 are a pair of amplification primers and SEQ ID Nos. 3 and 4 are sequencing primers. Of these, SEQ ID NO. 1 is identical to SEQ ID NO. 3 and SEQ ID No. 2 is identical to SEQ ID NO. 4.

Thus the current claim really is drawn to a kit with two different primers. One of the two primers is exactly anticipated by De Beenhouwer et al. (WO 95/33851). The other primer is prima facie obvious over De Beenhouwer et al. in view of Heym et al (USPN. 5,851,763) and Foxall et al. (USPN. 5,985,569).

Prima Facie Case

The prima facie case of obviousness for the primer combination is based upon three references, DE Beenhouwer et al. (WO 95/33851), Heym et al. (USPN. 5, 851, 763) and Foxall et al. (USPN. 5, 985, 569). De Beenhouwer et al. teach every limitation of the instant invention except for one sequence that of SEQ ID NO. 2 (and its identical version, SEQ ID 4). Heym et al. teach primers selected from sequence of the rpoB gene which comprise the instant SEQ ID No. 2 (SEQ ID No. 4), which is the target for antibiotic resistance in Mycobacterium tuberculosis. Foxall et al. teach a computer program to design suitable primers for amplification of the target gene sequence in Mycobacterium tuberculosis.

The Appellant did not dispute that the references teach and suggest each of the primer

sequences, but argue that the references did not teach or suggest the combination of the primer pair for amplification and sequencing. The appellant further argues that it is improper to rely on the obviousness of primer designing techniques, since the claims are directed to the combination of specific primer pair. The arguments directed to a specific combination of a primer pair should be found unpersuasive.

Motivation

In addressing the motivation issue, it is important to appreciate how routine and ordinary is the selection of a particular primer pair for amplification of a target gene of interest as taught be Heym et al. and Foxall et al. The technique to make the primer or end result is obvious at the time the invention was made and hence the product developed based on the known technique that is, oligo-design station (Foxal et al.) would be obvious, once the target gene sequence (rpoB gene) is known it is obvious to design a proper combination of primers flanking the target site to amplify the target. In the instant situation, the prior art teach the same gene target (rpoB gene of mycobacterium) whose sequence is known at the time the invention was made, and the prior art on record explicitly teches the significance of the target gene in antibiotic resistance, thus one having ordinary skill in the art would know how to design a primer or primers using the currently available techniques as described in the prior art (Heym et al. and Foxall et al), since RpoB gene target sequence is known in the art and the general techniques to design a primer is obvious from the know sequence.

The Appellant's analysis and arguments on pages 5-7 of the appeal brief, that references fail to properly combine the teachings of these primer selection techniques, are fully considered and found not persuasive. There is express suggestion in the prior art WO 95/33851, which teaches a kit comprising the sequences as claimed in SEQ ID Nos.1 and 3 which are

located on rpoB gene of mycobacterium and the patents US 5,851,763 and USPN. 5, 985, 569 teach a kit comprising primers having rpoB sequence that comprises the SEQ ID Nos. 2 and 4 as claimed in the instant invention and motivation to select specific primers.

There are no secondary considerations. Applicants have not shown any unexpexted result or a showing or a declaration supporting the arguments that the combination of the said primer pair and matching sequencing primers provide better results as compared to the prior art. It is proper to rely on the obviouness of primer selection techniques since the prior art suggests the small region for detection (rpoB gene) and suggest the use of these techniques (see Foxal et al.). The selection would have been obvious, since the prior art teaches rpoB gene sequence as a demostrated target sequence and the prior art provides guidance on how to design a proper combination of primers flanking the target site to amplify the target. In the instant situation, the prior art teaches the same gene target (rpoB gene of mycobacterium) with the same sequence and gene known at the time the invention was made, and since the prior art on record explicitly teaches the significance of the target gene in antibiotic resistance, one having ordinary skill in the art would know how to design a primer or primers using the currently available techniques as described in the prior art (Foxall et al), since RpoB gene target sequence is known in the art, the general techniques to design a combination of primers is obvious from the know sequence.

On Page 6, of the appeal brief Appellant argues that the specific combination of primers are not taught by the art, nor in the examiner's arguments and refers to a citation (US 6,228,577) which results in multiplicity of sequences, which appellant argues that the multiplicity of sequences are not one or two sequences. Appellant's' arguments are fully considered and found not persuasive. Appellant correctly pointed out multiplicity of primers can be designed,

however, of which certain primer sequences are selected based on melting temperatures, GC content and other factors suitable for routine experimentation. Thus not all possible primer sequences would be selected, however it is obvious that the target primer regions as demonstrated by the prior art would be selected to design the best set of primers because the prior art already established that the primers designed from those regions would positively work to produce the end result.

On page 7 of the appeal brief, Applicants' merely argues that the specific combination of primers as claimed in the instant invention are nonobvious and asserts that the case law of In re Deuel cited by the examiner was improper. The arguments are fully considered and found not persuasive. Applicants' argue only on one part of the case law that notes the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. The Appellant does not address the second part, which notes that with regard to structural or functional homologs, however, the court stated

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

Since the claimed primers simply represent structural homologs, which are suggested by the prior art as useful for primers and probes, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Thus it is more appropriate to cite the case law in the instant situation because the primers are homologs of a known rpo B gene.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.1992). In this case, specific motivation is provided in the rejection above, which notes An ordinary practitioner would have been motivated to combine the sequences of De Beenhouwer et al. with the primer sequences of Heym et al. and selection of primers of Foxall et al. in order to achieve the expected advantage of a sensitive kit composition for evaluating antibiotic resistance of mycobacterium species.

Conclusion

Therefore, an ordinary artisan would have recognized the expected benefits of designing a combination of primers based on the known primer target regions as demonstrated by the prior art, which would result in an improved detection system of the target gene. Further, Appellant does not provide factual evidence to support that the specific combination of primers would result in a better end results as compared to the prior art. Applicants have not shown any unexpexted result or a showing or a declaration supporting the arguments that the combination of the said primer pairs and matching sequencing primers provide better results as compared to the prior art. Therefore, for the above reasons, the rejection under U.S.C. 103(a) should be sustained.

Respectfully submitted,

Suryaprabha Chunduru
Examiner
Art Unit 1637

May 26, 2004

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